csas
Commissioning Support
Appraisals Service

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14th August 2012

National Institute for Health and Clinical Excellence

Dear [redacted]

RE: Ivabradine for the treatment of chronic heart failure

On behalf of the Commissioning Support Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for ivabradine for the treatment of chronic heart failure. We are in agreement with the recommendations in the ACD to recommend ivabradine for this indication as on the basis of the evidence considered it is likely that this treatment can be considered clinically and cost effective in real life clinical practice for the sub-group of patients specified in the ACD.

- **Ivabradine is an add-on therapy to standard care.** Ivabradine is proposed as an add-on therapy for the treatment of chronic heart failure in patients in sinus rhythm who are receiving standard care, for whom beta-blockers are contraindicated or who are receiving beta-blockers at maximally tolerated doses and who have a resting heart rate of 75 bpm or more.
- **Ivabradine reduced rates of cardiovascular death in a sub group of patients with a resting heart rate of 75 bpm or more.** In the SHIFT trial the rate of cardiovascular death or hospital admission for worsening heart failure (primary composite endpoint) in a subgroup analysis of patients with a resting heart rate of ≥75 bpm was statistically and clinically significant with ivabradine.
- **There were limitations to the quality of the research**. The manufacturer submitted effectiveness data based on the results of one well-designed and well-conducted international RCT. However, effectiveness in the population for which the manufacturer has marketing authorisation is based on the analysis of a subgroup (participants with a resting heart rate of 75 bpm or more (n=4,150)) identified retrospectively. Although no relevant baseline differences between the ivabradine and placebo groups were identified, the results should be interpreted with caution as this resting heart rate was not a stratification factor at randomisation.
- **The effectiveness of ivabradine in some patient populations is uncertain**. In the SHIFT trial only 26% of patients received the recommended dose of beta-blockers. There is uncertainty around the benefit of ivabradine plus standard care for patients with a resting heart rate of 75 bpm or more and who are receiving at least 25% of the recommended dose of beta-blockers. Ivabradine should only be initiated after four weeks of optimal standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists. The effectiveness of ivabradine in people with NYHA class IV heart failure is uncertain due to small patient numbers.

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- **Only patients with an ejection fraction of 35% or lower were included in the SHIFT trial.** Consideration should be given to whether only patients with an ejection fraction of 35% or lower should be considered for treatment with ivabradine.
- **The results from the SHIFT trial are generalisable to the UK population.** The Appraisal Committee and Evidence Review Group concluded that the results were robust and generalisable to the UK population despite the fact that participants in the SHIFT trial were younger and had more severe heart failure than the UK population, and that there were few UK participants.
- **Ivabradine is cost effective compared to treatments usually funded in the NHS, but is a costly alternative to standard care.** Although there were some uncertainties regarding the economic model, the Appraisal Committee concluded that the manufacturer's ICER estimate of approximately £8,500 per QALY was realistic. Based on manufacturers estimates a commissioner could expect to be asked to fund treatment for 66 patients per 100,000 population with ivabradine per year, which would equate to a cost of about £2,778.60 per month per 100,000 population or £33,343.20 per year per 100,000 population in addition to the cost of standard care.

If you require any further information please contact me directly: Phone: [redacted], email [redacted]

Yours sincerely

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